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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,921	12/22/2000	Kevin J. Thorne	2265-15	2764

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EXAMINER

LEITH, PATRICIA A

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/746,921

**Applicant(s)**

THORNE ET AL.

**Examiner**

Patricia Leith

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10, 24-29 and 32-48 is/are pending in the application.
- 4a) Of the above claim(s) 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10, 24-29 and 32-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

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### **DETAILED ACTION**

Claims 1-10 and 24-29 and 32-48 are pending in the application. Claim 9 has been withdrawn from the merits as being directed toward a non-elected invention.

Claims 1-8, 10, 24-29 and 32-48 were examined on the merits.

### ***Election/Restrictions***

Applicant's arguments concerning the restriction requirement were fully considered. It is noted that a restriction requirement in the Instant case was proper for the following reason; MPEP 818.02(b) states that "Where only generic claims are first presented and prosecuted in an application in which no election of a single invention has been made, and applicant later presents species claims to more than one species of the invention, he or she must at that time indicate an election of a single species. The practice of requiring election of species in cases with only generic claims of the unduly extensive and burdensome search type is set forth in MPEP § 808.01(a). However, the Examiner has reconsidered the restriction requirement, and deemed that the species are obvious variants of each other because all types of collagen are so similar in structure and function.

### ***Claim Rejections - 35 USC § 103***

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, 8, 10, 24-27, 32-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohura et al (1999) in view of Chen et al. (US 5,707,962).

The teachings of Ohura et al. were keenly described in previous Office Actions.

Ohura et al. did not specifically teach the incorporation of any type of collagen into the artificial bone matrix or the particular amounts of collagen in the composition.

Collagen matrices were well known in the art to be used as bone formation foundations as indicated by Chen et al. Chen et al. clearly teach that collagen matrices may be advantageously combined with calcium bone compositions as well as osteogenic factors such as TGF- $\beta$  (See col.3, lines 22-58 for example) to create bone growth compositions. Chen et al. specifically taught that the preferred collagen could be collected from bovine or human and could be tendon collagen (col.6, lines 35).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the instant ingredients for their known benefit

since each is well known in the art for bone growth and repair. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations of collagen because concentration is an art-recognized result-effective variable which would have been routinely determined and optimized in the pharmaceutical art.

Claims 1-8, 10 and 28-29 remain rejected and claims under 35 U.S.C. 103(a) as being unpatentable over Kwan et al. (US 6,187,047 B1) in view of Constantz (US 5,047,031) for the reasons of record.

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The Declaration submitted 5/18/04 was fully considered. The Declaration explains the experiments found in the Instant specification and points out the beneficially of the use of acidic calcium phosphate salts in the formation of bone as characterized by explant mass, histology, mineral concentration and mineral mass. Applicant summarizes the Declaration by contending that the "acidic calcium phosphate compositions are unexpectedly efficacious in accentuating bone protein induced growth", whereby Ohura et al., Constantz and Kwan et al. do not disclose this unexpected result.

Similarly, in the Arguments section on pages.12-13, Applicants contend that it was not known in the art that acidic calcium phosphate compositions enhanced bone growth: "Although Constantz states that the particular mineral will be affected by the pH and that the pH of the mixture will generally be in the range of about 5-8....the pH of the composition appears to merely reflect of the particular calcium/phosphate ratio employed to achieve the desired physical and mechanical properties of a composition....However, Constantz neither recognizes a relationship there between nor teaches anything about the enhancement of bone growth induced by any protein via a composition comprising an acidic pH". Although Constantz did not recognize the advantage of the composition being at a pH from about 5 to 8, *the pH was none-the-less within or overlapping the ranges as Instantly claimed*. Thus giving rise to further evidence that bone compositions comprising acidic calcium phosphate compositions; i.e., calcium monophosphate, will buffer in the acidic range. The ordinary artisan would

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have recognized that ingredients such as collagen and bone growth factors (bmp's for example) would not have changed the pH of the composition because these compounds do not release ions into solution. Absent other readily soluble salts in the composition which would affect buffering capacity (as well as any deliberate titration step to change the pH of the bone compositions comprising calcium phosphates), it is clear that the calcium phosphate compositions are the principal ingredient governing the pH of the mixture.

It is also noted that the rejection which includes Constanz is a rejection under 35 USC 103(a) and not under 35 USC 102(a). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, Applicant does contend that Constanz disclosed acidic calcium phosphate salts for use in bone construction which have pH's in the ranges as instantly claimed. Applicant is also contending, with regard to the Arguments, as well as the Declaration, that the addition of acidic calcium phosphates to bone construction material enhances bone formation parameters as discussed *supra*. The Examiner agrees that the Instant specification shows some enhanced properties of acidic calcium phosphates on bone repair. However, it is also known, as admitted by Applicant, that acidic calcium phosphates were already known in the art for aiding in bone repair. Therefore, Applicant has discovered an advantage of a

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use for a material that was already being used in the art for the analogous purpose. It is clear, as stated by Applicants, that the studies conducted on the acidic calcium phosphates included the controls of collagen and bone protein; thereby rendering an alleged 'unexpected result', as contended by Applicants, to the acidic calcium phosphate compounds themselves, and not some unobvious combination of elements.

Again, it is deemed that the inclusion of acidic calcium phosphates into a bone composition comprising *known* bone construction additives such as collagen and bone proteins would have been obvious to one of ordinary skill in the art because all of the ingredients were known to aid in bone repair. **The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.** See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant has noted that monocalcium phosphate actually has a pKa of 4.2, whereby the Examiner had estimated the pKa of monocalcium phosphate based upon the pKa of hydrogen phosphate. Applicant's pKa of monocalcium phosphate is accepted as correct. Applicant states that the buffering range of calcium phosphate is in the range of 3.2 to 5.2. It is noted that this range falls within the claimed ranges, or very close to the claimed ranges. Because both rejections include the acidic calcium phosphate compositions of calcium monophosphate, it is deemed that the references

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make obvious the claimed pH ranges. It is also noted that in both rejections cited *supra*, none of the references triturate the final product to a basic pH. Because the calcium phosphate compositions comprise good buffering capacities as discussed in previous Office Actions, it remains deemed that the compositions would have afforded pH's as recited in the claims (as can be seen by the buffering ranges of monocalcium phosphate as well as dicalcium hydrogen phosphate recited in the Declaration). This is further evidenced in the rejection over Constanz who clearly teaches that the pH of the composition was from 5-8. Applicant argues that at the time the Instant invention was made, that the common knowledge in the art was to create bone compositions at alkaline pH's. However, Constanz clearly taught that the composition comprising acidic calcium phosphates such as brushite would have had a pH of about 5-8, wherein a pH of 5-6 is considered 'acidic'. Because this range overlaps the acidic pH range, the reference tends to negate the contention of the Applicant; that bone compositions were made and used in the acidic pH range. Again, none of the references state that the compositions were buffered to an alkaline pH.

It is finally noted that claim 2 has been amended to recite calcium hydrogen phosphate dihydrate which limits the 'acidic calcium phosphate' which was previously recited in the claims. Calcium hydrogen phosphate dihydrate is also known as 'brushite', a calcium phosphate composition already disclosed by Constanz as being a suitable calcium phosphate composition for bone construction. Again, Constanz clearly

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stated that the pH of the composition was from 5-8 thereby rendering the claimed invention obvious.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith  
Primary Examiner  
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A handwritten signature in black ink, appearing to read 'Patricia Leith', with a stylized flourish at the end.

11/17/04